

Application No. 09/821,694

Amendment dated

Reply to final Office Action of December 14, 2004

EXPEDITED PROCEDURE - GROUP ART UNIT 1634

Att Dkt No. 0450-0001

**AMENDMENTS TO THE CLAIMS**

The following listing of the claims replaces all prior versions and listings of the claims for this application. Within this listing of the claims, claims 1, 7, 10, 29, 117, and 118 are amended and claim 116 is canceled.

1. **(Currently amended)** A method of employing oligonucleotide probes to obtain information on a position of interest on a target sequence segment of a target nucleic acid analyte, the method comprising:

contacting the target nucleic acid analyte, under hybridizing conditions, with at least two oligonucleotide probes ~~that are identical to each other except for a single~~ having a variable position,

wherein on at least one of the at least two oligonucleotide probes, the variable position is occupied by a ~~degenerate~~ degenerately base pairing nucleotide analog selected from the group consisting of dP and 8-oxo-dG and on at least one other of the at least two oligonucleotide probes, the variable position is occupied by a degenerately base pairing nucleotide analog selected from the group consisting of dP and 8-oxo-dG or a non-degenerately base pairing nucleotide;

wherein hybridization of one or all of the at least two oligonucleotide probes to the target sequence segment occurs only if the degenerately base pairing nucleotide analog or the non-degenerately base pairing nucleotide at the variable position base pairs with a complementary nucleotide at the position of interest; and

further wherein none of the at least two oligonucleotide probes hybridizes to the target nucleic acid analyte if there is a mismatch between the degenerately base pairing nucleotide analog or the non-degenerately base pairing nucleotide at the variable position and a nucleotide at the position of interest on the target sequence segment.

2-5. **(Canceled)**

6. **(Previously presented)** The method of claim 1 used for sequencing the target nucleic acid analyte.

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7. **(Currently amended)** The method of claim 6 further comprising an array of oligonucleotide probes, wherein ~~the target sequence segment of the target nucleic acid analyte~~ hybridizes to the array of oligonucleotide probes and further wherein the target sequence of the target nucleic acid analyte is determined by analysis of hybridization data obtained from the array of oligonucleotide probes.

8. **(Original)** The method of claim 7 wherein the array comprises arrayed individual beads or particles, each bead or particle having a surface to which is attached a plurality of oligonucleotide probes of identical sequence.

9. **(Original)** The method of claim 7 wherein the array comprises a substrate having a surface, the surface having a plurality of discrete surface sites, each site having attached a plurality of oligonucleotide probes of identical sequence.

10. **(Currently amended)** The method of claim 7 wherein ~~the target sequence segments segment hybridized to the array of oligonucleotide probes are~~ is detected by a discrete label moiety linked to the target sequence segment.

11. **(Original)** The method of claim 10 wherein the discrete label moiety linked to the target sequence segment comprises a nucleic acid sequence.

12. **(Original)** The method of claim 10 wherein the discrete label moiety linked to the target sequence segment comprises a luminescent moiety.

13. **(Original)** The method of claim 12 wherein the luminescent moiety is a chemiluminescent or fluorescent moiety.

14. **(Previously presented)** The method of claim 9 wherein the target sequence segment is detected by a target signal.

15. **(Previously presented)** The method of claim 14 wherein the target signal is <sup>32</sup>P.

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16. **(Previously presented)** The method of claim 7 wherein target sequence segments hybridized to the array of oligonucleotide probes are detected by measuring hybridization temperature.

17. **(Previously presented)** The method of claim 6 wherein the target nucleic acid analyte is sequenced by detection of labels that attach by hybridization to the target sequence segments of the target nucleic acid analyte.

18. **(Previously presented)** The method of claim 1 wherein the target nucleic acid analyte is amplified by a polymerase enzyme.

19. **(Previously presented)** The method of claim 18 wherein the target nucleic acid analyte is amplified by polymerase chain reaction.

20. **(Previously presented)** The method of claim 18 wherein the target nucleic acid analyte is amplified by an RNA replicase enzyme.

21. **(Previously presented)** The method of claim 19 used for genetic analysis.

22. **(Previously presented)** The method of claim 1 used for allelic analysis.

23. **(Previously presented)** The method of claim 1 wherein the target nucleic acid analyte is derived from genomic DNA.

24. **(Previously presented)** The method of claim 1 wherein the target nucleic acid analyte is derived from a cDNA.

25-26. **(Canceled)**

27. **(Previously presented)** The method of 6 wherein the target nucleic acid analyte is sequenced by analysis of hybridization data obtained from the target sequence segments attached to a substrate surface.

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28. **(Previously presented)** The method of 14 wherein the array is comprised of individual beads or particles, each bead or particle having a surface to which are attached a plurality of identical target sequence segments.

29. **(Currently amended)** The method of 14 wherein the array comprises an integrated substrate with a surface comprised of discrete sites, each site having a surface, the surface having attached a plurality of target sequence segments having an identical sequence.

30. **(Previously presented)** The method of claim 14 wherein individual oligonucleotide probes in the array are further comprised of a linker moiety and a label moiety.

31. **(Previously presented)** The method of claim 30 wherein the linker moiety comprises a common nucleic acid sequence and the label moiety comprises a signature nucleic acid sequence that identifies the target sequence segment.

32. **(Canceled)**

33. **(Previously presented)** The method of claim 31 wherein the array is imaged with decoder labels comprising a nucleic acid sequence complementary to the signature nucleic acid sequence and a second label moiety.

34. **(Previously presented)** The method of claim 33 wherein the second label moiety comprises a luminescent moiety.

35. **(Original)** The method of claim 34 wherein the luminescent moiety is a fluorescent or chemiluminescent moiety.

36. **(Original)** The method of claim 14 wherein the substrate surface is functionalized with a surface modification to enhance hybridization.

37. **(Previously presented)** The method of claim 36 wherein the hybridization is enhanced by increasing hybridization stringency.

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38. **(Previously presented)** The method of claim 29 wherein hybridization of the target nucleic acid analyte to the array is enhanced by electronically controlling electric potential at the substrate surface.

39. **(Previously presented)** The method of claim 29 wherein the integrated substrate comprises a semiconductor chip comprising electronic circuitry, wherein electric potential at the individual array sites of the substrate surface is independently electronically controlled to enhance hybridization.

40-115. **(Canceled).**

116. **(Canceled)** ~~The method of claim 1 wherein the degenerately pairing nucleotide analog is selected from the group consisting of dP and 8-oxo-dG.~~

117. **(Currently amended)** The method of claim 1 wherein the target nucleic acid analyte is DNA and the ~~variable nucleotide of the at least two oligonucleotide probes~~ non-degenerately base pairing nucleotide is independently selected from the group consisting of A, T, C, and G.

118. **(Currently amended)** The method of claim 1 wherein the target nucleic acid analyte is RNA and the non-degenerately base pairing nucleotide is independently selected from the group consisting of A, U, C, ~~or~~ and G.